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TLR7 gene effect on hepatic fibrosis progression rate in HIV-infected patients with chronic hepatitis C

L. M. Syzova*[1,A–E], T. I. Koval[1,A–F], L. P. Kotsiubailo[2,A,D,E], O. H. Marchenko[1,A,D,E]

[1]Ukrainian Medical Stomatological Academy, Poltava, [2]Shupyk National Medical Academy of Postgraduate Education, Kyiv, Ukraine

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

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***E-mail:** isizof@gmail.com

The aim of the research – to optimize the prediction of hepatic fibrosis (HF) progression rate in HIV-infected patients with chronic hepatitis C (CHC) based on a comprehensive assessment of general clinical, biochemical, immunological and molecular-genetic markers.

Materials and methods. A cross-sectional cohort study was conducted, which included 104 HIV-infected patients with CHC. The examination program included: assessment of complaints and anamnestic data obtained by questioning and detailed analysis of medical records, physical examination, general clinical study of peripheral blood, determination of biochemical parameters of blood serum, characterizing the functional state of the liver, the level of CD4+ T-lymphocytes, the stages of HF according to METAVIR and genetic studies (genotyping of TLR7 in order to determine the carriage of Leu allele).

Results. The method of discriminant analysis showed that statistically significant informative diagnostic signs of the rapid rate of HF progression in HIV-infected patients with CHC are: lymphocytosis, the levels of AST and total bilirubin exceeding the upper limit of normal, among the concomitant pathology – chronic cholecystitis, chronic pancreatitis, cholelithiasis and hepatic steatosis, the baseline level of CD4+ T-lymphocytes less than 350 cells/mm^3 and a carriage of the normal genotype (Gln/Gln, Gln/-) of the TLR7 gene. In order to optimize the prognostication of the affiliation of an HIV-infected patient with CHC to the risk group of HF rapid progression there was proposed a discriminant model of 5 risk factors (the normal genotype (Gln/Gln, Gln/-) of the TLR7 gene, the levels of total bilirubin and AST exceeding the upper limit of normal, lymphocytosis, the baseline level of CD4+ T-lymphocytes less than 350 cells/mm^3), the exact prognosis of which was 75 %.

Conclusions. There was proposed an effective model that allows predicting a rapid rate of HF progression in HIV-infected patients with CHC on the basis of simple characteristics, most of which are used in routine clinical practice.

Ключові слова: ВІЛ-інфекція, хронічний гепатит С, фіброз печінки, прогноз.

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Вплив гена TLR7 на темп прогресування фіброзу печінки у ВІЛ-інфікованих пацієнтів із хронічним гепатитом С

Л. М. Сизова, Т. І. Коваль, Л. П. Коцюбайло, О. Г. Марченко

Мета роботи – оптимізувати прогнозування темпу прогресування фіброзу печінки (ФП) у ВІЛ-інфікованих пацієнтів із хронічним гепатитом С (ХГС) на основі комплексного оцінювання загальноклінічних, біохімічних, імунологічних і молекулярно-генетичних маркерів.

Матеріали та методи. Здійснили крос-секційне когортне дослідження, в яке залучили 104 ВІЛ-інфікованих пацієнти з ХГС. Програма обстеження передбачала оцінювання скарг та анамнестичних даних, що отримали під час опитування та детального аналізу медичної документації, фізикальний огляд, загальноклінічне дослідження периферичної крові, визначення біохімічних показників сироватки крові, що характеризують функціональний стан печінки, рівня CD4+ Т-лімфоцитів, стадії ФП за METAVIR і генетичні дослідження (генотипування TLR7 для визначення носійства поліморфного алеля Leu).

Результати. Методом дискримінантного аналізу встановили, що статистично вірогідними інформативними діагностичними ознаками швидкого темпу прогресування ФП у ВІЛ-інфікованих пацієнтів із ХГС є лімфоцитоз, рівні АСТ і загального білірубіну, які перевищують верхню межу норми, серед супутньої патології – хронічний холецистит, хронічний панкреатит, жовчнокам'яна хвороба і стеатоз печінки, вихідний рівень CD4+ Т-лімфоцитів менше ніж 350 кл/мкл і носійство нормального генотипу (Gln/Gln, Gln/-) гена TLR7. Для оптимізації прогнозування належності ВІЛ-інфікованого пацієнта з ХГС до групи ризику швидкого прогресування ФП запропонована дискримінантна модель із 5 факторів ризику (нормальний генотип гена TLR7 (Gln/Gln, Gln/-), рівні загального білірубіну та АСТ, котрі перевищують верхню межу норми, лімфоцитоз, вихідний рівень CD4+ Т-лімфоцитів менше ніж 350 кл/мкл), безпомилковий прогноз якої становив 75 %.

Висновки. Запропоновано ефективну модель, що дає змогу прогнозувати швидкий темп прогресування ФП у ВІЛ-інфікованих пацієнтів із ХГС на основі простих характеристик, більшість із яких використовують у рутинній клінічній практиці.

Влияние гена TLR7 на темп прогрессирования фиброза печени у ВИЧ-инфицированных пациентов с хроническим гепатитом С

Л. М. Сизова, Т. И. Коваль, Л. П. Коцюбайло, Е. Г. Марченко

Цель работы – оптимизировать прогнозирование темпа прогрессирования фиброза печени (ФП) у ВИЧ-инфицированных пациентов с хроническим гепатитом С (ХГС) на основе комплексной оценки общеклинических, биохимических, иммунологических и молекулярно-генетических маркеров.

Материалы и методы. Проведено кросс-секционное когортное исследование, в которое вошли 104 ВИЧ-инфицированных пациента с ХГС. Программа обследования включала оценку жалоб и анамнестических данных, полученных при опросе и детальном анализе медицинской документации, физикальный осмотр, общеклиническое исследование периферической крови, определение биохимических показателей сыворотки крови, характеризующих функциональное состояние печени, уровня CD4+ Т-лимфоцитов, стадии ФП по METAVIR и генетические исследования (генотипирование TLR7 для определения носительства аллели Leu).

Результаты. Методом дискриминантного анализа установлено, что статистически достоверными информативными диагностическими признаками быстрого темпа прогрессирования ФП у ВИЧ-инфицированных пациентов с ХГС являются лимфоцитоз, уровни АСТ и общего билирубина, превышающие верхнюю границу нормы, среди сопутствующей патологии – хронический холецистит, хронический панкреатит, желчекаменная болезнь и стеатоз печени, исходный уровень CD4+ Т-лимфоцитов менее 350 кл/мкл и носительство нормального генотипа (Gln/Gln, Gln/-) гена TLR7. Для оптимизации прогнозирования принадлежности ВИЧ-инфицированного пациента с ХГС к группе риска быстрого прогрессирования ФП предложена дискриминантная модель из 5 факторов риска (нормальный генотип гена TLR7 (Gln/Gln, Gln/-), уровни общего билирубина и АСТ, превышающие верхнюю границу нормы, лимфоцитоз, исходный уровень CD4+ Т-лимфоцитов менее 350 кл/мкл), безошибочный прогноз которой составил 75 %.

Выводы. Предложена эффективная модель, которая позволяет прогнозировать быстрый темп прогрессирования ФП у ВИЧ-инфицированных пациентов с ХГС на основе простых характеристик, большинство из которых используют в рутинной клинической практике.

Ключевые слова: ВИЧ-инфекция, хронический гепатит С, фиброз печени, прогноз.

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Relevance

HIV infection and chronic hepatitis C (CHC) are the most important problems of modern infectious diseases [1–4]. Combined HIV/CHC infection promotes the progression of liver damage, increases the risk of side effects of antiretroviral therapy, and to date CHC remains one of the main causes of mortality among HIV-infected people, except opportunistic diseases [3–5]. The prognosis of CHC is based on the idea about the rate of fibrosis progression (RFP), as patients with a rapid rate of hepatic fibrosis (HF) transformation into cirrhosis require the individualization of therapeutic and diagnostic approach. This issue is especially relevant for the reasonable selection of patients who need immediate appointment of antiviral therapy of CHC in conditions of limited access to it.

Recently, there has been an active search for genetic determinants, which affect RFP, in particular, TLR7 gene, the ligand of which is viral RNA, is studied [3,6–9]. It is known that this gene predominantly regulates the production of type I interferons, which have antifibrotic effect [6,10]. It is of interest to study the influence of TLR7 gene Gln/Leu polymorphism on the rate of HF progression, since the scientific data concerning this process dependence on the carriage of the Leu allele in patients with CHC are inconsistent, and in HIV/CHC-coinfected – extremely limited [11–15].

Thus, a study, that would assess the risk of rapid progression of HF in HIV-infected patients with CHC based on complex analysis and comparison of genetic markers with clinical data, is an actual scientific and practical task.

The aim of the study

To optimize the prediction of HF progression rate in HIV-infected patients with CHC based on a comprehensive assessment of general clinical, biochemical, immunological and molecular-genetic markers.

Materials and methods

To achieve this goal, a cross-sectional cohort study was conducted, which included 104 HIV-infected patients with CHC: men – 77 (74.0 %) and women – 27 (26.0 %) in the age range of 28 to 55 years, median *(Me)* = 39.0 (36.0–44.0). Complex clinical and laboratory examination was conducted on the bases of Poltava Regional Clinical Hospital of Infectious Diseases, Poltava Regional HIV/AIDS Prevention and Control Center and in Commercial Laboratories according to the informed consent of the patients.

The diagnosis of CHC and HIV infection was established according to the International Classification of Diseases of the 10th revision, verified by the detection of specific serological and molecular-biological markers of these infections (antibodies to HCV and HIV by the method of ELISA, HCV RNA with genotyping, viral load (VL) of HCV and HIV by PCR method in real time (RT-PCR), high for HCV counted viremia over $4.0 \cdot 10^5$ IU/ml, for HIV – more than $1.0 \cdot 10^5$ IU/ml).

The patient examination program included: assessment of complaints and anamnestic data obtained by questioning and detailed analysis of medical records, physical examination, general clinical study of peripheral blood, determination of biochemical parameters of blood serum, characterizing the liver functional state, the level of $CD4^+$ T-lymphocytes, the stages of HF according to METAVIR and genetic studies (genotyping of TLR7 in order to determine the carriage of Leu allele). The frequency of concomitant pathology was established based on the results of anamnesis analysis, outpatient cards, objective examination followed by in-depth clinical, laboratory and instrumental studies, findings of specialists in related specialties.

The duration of HCV infection was determined by the results of anamnestic data analysis (indication of the suffered icteric form of acute hepatitis C, transfusion of blood and its components prior to mandatory screening of donors, initiation of systemic injecting drug use), in the absence of these facts anamnesis – on the basis of clinical and laboratory data (the first detection of antibodies to HCV and/or the level of hepatic transaminases exceeding the upper limit of normal (ULN), reflected in outpatient cards).

Biochemical studies were carried out on the automatic biochemical analyzer GBG STAT FAX-1904 (Japan) by the HUMAN's reagents (Germany).

The level of $CD4^+$ T-lymphocytes was determined by flow cytometry using the BD FACSCalibur analyzer and test systems (BD Biosciences, USA).

The HF stage was assessed on the METAVIR scale using the FibroTest methods on a Cobas 6000 analyzer (with

Table 1. Potential risk factors for the rapid rate of hepatic fibrosis progression in HIV-infected patients with chronic hepatitis C

Factors	Presence of factor, abs. (%)		F	P
	Rapid rate of HF progression (n = 52)	Slow rate of HF progression (n = 52)		
Male gender (1 – yes, 0 – no)	41 (78.8)	36 (69.2)	1.24	0.268
Age over 40 years (1 – yes, 0 – no)	23 (44.2)	22 (42.3)	0.03	0.845
Overweight, BMI ≥25 kg/m^2 (1 – yes, 0 – no)	11 (21.2)	11 (21.2)	0.00	1.0
Ethanol consumption > 40 g/day (1 – yes, 0 – no)	17 (32.7)	12 (23.1)	1.16	0.279
Tobacco smoking (1 – yes, 0 – no)	40 (76.9)	38 (73.1)	0.20	0.654
Use of intravenous drugs (1 – yes, 0 – no)	39 (75.0)	36 (69.2)	0.42	0.516
1 genotype of HCV (1 – yes, 0 – no)	25 (48.1)	29 (55.8)	0.60	0.437
High VL HCV (1 – yes, 0 – no)	24 (46.2)	23 (44.2)	0.03	0.846
High VL HIV (1 – yes, 0 – no)	18 (34.6)	12 (23.1)	1.68	0.198
Concomitant pathology of the gastrointestinal tract (1 – yes, 0 – no), including:	47 (90.4)	35 (67.3)	8.84	0.004
– chronic cholecystitis	30 (57.7)	16 (30.8)	8.08	0.005
– chronic pancreatitis	26 (50.0)	15 (28.8)	5.01	0.027
– chronic gastroduodenitis	22 (42.3)	15 (28.8)	2.05	0.155
– chronic duodenal ulcer	8 (15.4)	4 (7.7)	1.50	0.223
– cholelithiasis	7 (13.5)	1 (1.9)	5.01	**0.027**
– hepatic steatosis	9 (17.3)	1 (1.9)	7.45	**0.007**
Extrahepatic manifestations of CHC (1 – yes, 0 – no), including:	3 (5.8)	4 (7.7)	1.06	0.304
– type II diabetes mellitus	1 (1.9)	1 (1.9)	0.00	1.0
– autoimmune thyroiditis	1 (1.9)	3 (5.8)	1.03	0.312
– glomerulonephritis	1 (1.9)	1 (1.9)	0.00	1.0
Erythropenia (1 – yes, 0 – no)	14 (26.9)	11 (21.2)	0.46	0.496
Low hemoglobin (1 – yes, 0 – no)	9 (17.3)	8 (15.4)	0.06	0.793
Leukopenia (1 – yes, 0 – no)	9 (17.3)	14 (26.9)	1.38	0.242
Lymphocytosis (1 – yes, 0 – no)	35 (67.3)	18 (34.6)	12.21	0.001
Monocytosis (1 – yes, 0 – no)	8 (15.4)	5 (9.6)	0.78	0.379
Rise in ESR (1 – yes, 0 – no)	16 (30.8)	14 (26.9)	0.18	0.669
Thrombocytopenia (1 – yes, 0 – no)	15 (28.8)	10 (19.2)	1.30	0.255
ALT level up to 3 ULN (1 – yes, 0 – no)	32 (61.6)	30 (57.7)	0.04	0.843
ALT level above 3 ULN (1 – yes, 0 – no)	11 (21.2)	5 (9.6)	2,67	0,105
AST level above ULN (1 – yes, 0 – no)	39 (75.0)	29 (55.8)	7.46	0.007
GGT level above ULN (1 – yes, 0 – no)	32 (61.5)	27 (51.7)	1.91	0.169
Total bilirubin level above ULN (1 – yes, 0 – no)	22 (42.3)	10 (19.2)	6.80	0.010
Alkaline phosphatase level above ULN (1 – yes, 0 – no)	8 (15.4)	3 (5.8)	2.55	0.113
Baseline level of CD4+ T-lymphocytes less than 350 cells/mm^3 (1 – yes, 0 – no)	41 (78.8)	30 (57.7)	5.55	0.020
Baseline level of CD4+ T-lymphocytes less than 200 cells/mm^3 (1 – yes, 0 – no)	27 (51.9)	21 (40.4)	1.38	0.242
Genotype of the TLR7 gene (1 – Gln/Gln, Gln/-, 0 – Gln/Leu, Leu/Leu and Leu/-)	46 (88.5)	31 (59.6)	12.37	0.001

a 501 module) using the Roche Diagnostics (Switzerland) test systems and shear wave transient elastometry of the liver on the ultrasound scanning device "Ultima PA-Expert" (Ukraine). The RFP was calculated by T. Poynard's formula by dividing the stage of HF by METAVIR for the time, during which it was formed, and measured in units per year (units/year) [16].

RFP in each of the examined was calculated and its *Me* was determined, which was 0.151 (0.045–1.000) units/year and afterwards, the groups of patients with rapid (RFP > 0.151 units/year) and slow (RFP ≤ 0.151 units/year) rate of HF progression were defined – 52 people from each group.

Polymorphic region of Gln/Leu gene TLR7 was genotyped by real-time allele-specific PCR on the "DT Lite" amplifier (JSC "NPO DNA-Technology", RF).

Statistical processing of the findings was carried out using the program SPSS 17.0 (USA). Consistency of the data characterized by a normal distribution was verified using the Kolmogorov–Smirnov criterion. To determine the central trend, the value of the *Me* with the upper and lower quartiles was used. As potential risk factors of the rapid rate of HF progression in HIV-infected patients with CHC, 35 indicators (results of general clinical, biochemical, immunological and molecular-genetic studies) ranked in a nominal scale (1 – sign, 0 – none) were examined and analyzed. In order to select the most informative signs, each method was evaluated by a single-factor analysis of variance. To create a mathematical model for predicting the rate of HF progression, the method of stepwise multiple discriminant analysis of Fisher was used, where the binary feature served as a grouping: 1 – rapid and 0 – slow rate of HF progression. In the course of the analysis, Wilks's lambda value was calculated, the informative value of each variable in the discriminant model (tolerance) and the efficiency of the obtained model. For all types of analysis, the level of difference was assumed to be statistically significant at $P < 0.05$.

Results

The study found a predominance of young and middle-aged subjects among the surveyed (76.9 %). According to the genotype of HCV and VL level, the patients were divided almost equally: 1 genotype – had 51.9 % of people, 2 and 3 – 48.1 %, high and low levels – 45.2 % and 54.8 %, respectively. The duration of HCV infection was 1 to 25 years: less than 5 – 8.6 %, 5 to 10 – 26.0 %, more than 10 – 65.4 %, *Me* = 14.0 (8.0–17.0). At the time of the examination, different stages of HF were determined in patients on the METAVIR scale with prevalence of F_2: F_0 – 10.6 %, F_1 – 18.3 %, F_2 – 42.3 %, F_3 – 23.1 % and F_4 – 5.8 %.

As a result of the genetic study, it was found out that normal carriers were registered among the patients: women – Gln/Gln (44.4 %), men – Gln/- (84.4 %), and polymorphic: women – Gln/Leu (51.9 %) and Leu/Leu (3.7 %), men – Leu/- (15.6 %) of the genotypes of the TLR7 gene. In general, the frequency of the Leu allele registration was 21.4 %.

In order to find informative signs of the rapid rate of HF progression in HIV-infected patients with CHC 35 variables were studied by the single-factor analysis of variance: biological (gender, age), behavioral (tobacco smoking, consumption of alcohol and intravenous drugs) associated with HCV and HIV (VL, genotype), as well as with the host organism (overweight – BMI ≥ 25 kg/m^2, concomitant pathology, extrahepatic manifestations of CHC indicators of general clinical, biochemical blood analysis and the degree of immunosuppression that was estimated at the baseline level of CD4+ T-lymphocytes) factors, supplemented with genetic markers (genotype TLR7 – Gln/Gln, Gln/-, Gln/Leu, Leu/Leu and Leu/-) (*Table 1*).

As can be seen from the data presented in *Table 1*, the following risk factors had a statistically significant effect on the rapid rate of HF progression in HIV-infected patients with CHC: lymphocytosis ($F = 12.21$, $P = 0.001$), the levels of AST and total bilirubin exceeding ULN ($F = 7.46$, $P = 0.007$

Table 2. Characteristics of the variables of the final discriminant model for predicting the rapid rate of hepatic fibrosis progression in HIV-infected patients with chronic hepatitis C

Sign	Wilks's lambda	F	p	Tolerance
Normal genotype (Gln/Gln, Gln/-) of the TLR7 gene	0.892	12.37	0.001	0.907
Total bilirubin level above ULN	0.794	13.09	0.000	0.901
Lymphocytosis	0.703	14.10	0.000	0.927
AST level above ULN	0.650	13.31	0.000	0.928
Baseline level of CD4+ T-lymphocytes less than 350 cells/mm^3	0.601	13.01	0.000	0.939

and F = 6.80, P = 0.010, respectively), the concomitant gastrointestinal tract pathology (F = 8.84, P = 0.004), in particular – chronic cholecystitis (F = 8.08, P = 0.005), chronic pancreatitis, cholelithiasis (F = 5.01, P = 0.027 for both indicators) and hepatic steatosis (F = 7.45, P = 0.007), the baseline level of CD4+ T-lymphocytes less than 350 cells/mm^3 (F = 5.55, P = 0.020). The carrier genotype (Gln/Gln, Gln/-) of the TLR7 gene (F = 12.37, P = 0.001) also proved to be a profibrogenic genetic marker, and the availability of the Leu allele of the gene in the genome, accordingly, a protective factor in relation to the rapid rate of HF progression.

Thus, it was found that among the 35 possible risk factors for the rapid rate of HF progression in HIV-infected patients with HCV, 9 had the greatest impact. These factors were included in a stepwise multiple discriminant analysis, the purpose of which was to construct functions that, in an optimal set of variables, predict the assignment of a patient to a group of rapid or slow progression of HF in HIV-infected patients with CHC. The formation of such groups is important for predicting the disease and prioritizing the appointment of antiviral therapy to patients.

The final discriminant model obtained as a result of the analysis included 5 features, each of which had a high statistical significance and a high informative index (*Table 2*).

The resulting classification linear discriminant functions (F_r and F_s) made it possible to predict the rapid or slow rate of HF progression in HIV-infected patients with CHC by a combination of characteristics using the coefficients obtained in the course of the analysis:

$$F_r = -10.38 + 6.88 \cdot X_1 + 3.73 \cdot X_2 + 5.17 \cdot X_3 + \\ + 5.31 \cdot X_4 + 5.25 \cdot X_5;$$

$$F_s = -4.70 + 4.44 \cdot X_1 + 1.95 \cdot X_2 + 2.97 \cdot X_3 + \\ + 3.58 \cdot X_4 + 3.66 \cdot X_5,$$

X_1: normal genotype of TLR7 gene (Gln/Gln, Gln/-), X_2: total bilirubin level above ULN, X_3: lymphocytosis, X_4: AST level above ULN, X_5: baseline level of CD4+ T-lymphocytes less than 350 cells/mm^3 (if there is a characteristic, a coefficient of 1 is added, if it is absent – 0).

A function, which mathematically calculated value is higher, indicates a patient belonging to a group: in $F_r > F_s$, a rapid rate is predicted, and in $F_r < F_s$ – a slow rate of HF progression in HIV-infected patients with CHC.

The accurate forecast of the obtained models was 75.0 % (for rapid rate of progression – 84.6 %, for slow – 65.4 %), which proves the high efficiency and expediency of their practical application with the aim to optimize the prediction of HF progression rapid rate in HIV-infected patients with CHC on the basis of simple characteristics, most of which are used in routine clinical practice.

Discussion

Nowadays, HF is considered as a process when some number of extraneous factors interacts with a unique combination of the host's ones and causes significant differences in a natural course of CHC. Among generally accepted factors of HF progression – some of them were confirmed by the results of research – there are virus factors (genotype and quasispecies of CHC, level of VL), host factors (duration of the disease, age at the moment of infection >40 years, male sex, co-infection with HBV or/and HIV, concomitant diseases of the gastrointestinal tract, metabolic factors (insulin resistance, hepatic steatosis, type II diabetes mellitus, disorders of iron metabolism, genetic background), and extraneous (ethanol consumption >40 g/day, effects of toxic substances, and, in particular, drugs, tobacco smoking, smoking cannabis derivatives) [16-18].

Despite the similarity between HIV and HCV, there are large differences between these viruses, which are related to target-cells. Thus, HIV attacks T-cells CD4+ and HCV – hepatocytes. In case of co-infection, a synergistic action of the viruses on the target-cells occurs that leads to development of more serious clinical manifestations and acceleration of the liver injury progression. Gradual reduction of CD4+ T-lymphocytes number that is associated with HIV-infection may potentially cause a decrease in specific immune response and a loss of control over HCV and the help function of intrahepatic T-helpers; thus increasing the number of infected hepatocytes and accelerating liver damage, and the existence of concomitant HIV-infection results in a fast rate of HF progression starting from the chronization of HCV-infection because of absence or low level of critically important cells for a response against HCV – CD4+ T-lymphocytes [19–22].

On the other hand, the redundant cytotoxic activity of lymphocytes that is caused by lymphocytosis contributes to damaging of liver cells in viral hepatitis's, and a nature of cytokines production by these cells determinates an intensity of fibrosis formation that leads to liver cirrhosis [21,23,24].

There are no doubts about data on the influence of increased levels of such functional indicators as AST and total bilirubin, because they are non-direct biochemical markers of fibrogenesis – they indicate activity of inflammation in liver tissues and disruption of its synthetic function and allow indirectly estimate an HF stage [25,26].

Along with universally recognized risk factors that have an influence on HF rate, significant role belongs to genetic markers [18]. The results of the study on the effect of TLR7 gene polymorphism on the rapid progression of HF in HCV and HIV/HCV co-infection are in line with a number of scientific studies [11,12,15]. Although E. Schott et al. (2007) reported a relation between the presence of the polymorphic genotype TLR7 and the process of fibrosis

in the liver exclusively in men [13], E. Ascar (2010) showed its absence [14].

Thus, the obtained results on the risk factors of a rapid rate of HF progression in HIV-infected patients with HCV, in general, are consistent with the data of world scientific literature and the prognostic model created on their basis will give an opportunity to optimize and individualize the therapeutic tactics in the disease.

Conclusions

1. Informative diagnostic signs of the rapid rate of HF progression in HIV-infected patients with CHC are: lymphocytosis (F = 12.21, P = 0.001), the levels of AST and total bilirubin exceeding ULN (F = 7.46, P = 0.007 and F = 6.80, P = 0.010, respectively), among the concomitant pathology – chronic cholecystitis (F = 8.08, P = 0.005), chronic pancreatitis, cholelithiasis (F = 5.01, P = 0.027 for both indicators) and hepatic steatosis (F = 7.45, P = 0.007), the baseline level of CD4+ T-lymphocytes less than 350 cells/mm^3 (F = 5.55, P = 0.020), as well as a carriage of the normal genotype (Gln/Gln, Gln/-) of the TLR7 gene (F = 12.37, P = 0.001).

2. In order to optimize the prognostication of the affiliation of an HIV-infected patient with CHC to the risk group of HF rapid progression there was proposed a discriminant model of 5 risk factors (the normal genotype (Gln/Gln, Gln/-) of the TLR7 gene, the levels of total bilirubin and AST exceeding ULN, lymphocytosis, the baseline level of CD4+ T-lymphocytes less than 350 cells/mm^3), the exact prognosis of which was 75.0 %.

Prospects for further research are to study the pathogenetic mechanisms of the TLR7 gene influence on the course of CHC in HIV-infected people.

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Information about authors:
Syzova L. M., MD, PhD, Assistant of the Department of Infectious Diseases with Epidemiology, Ukrainian Medical Stomatological Academy, Poltava.
Koval T. I., MD, PhD, DSc, Associate Professor of the Department of Infectious Diseases with Epidemiology, Ukrainian Medical Stomatological Academy, Poltava.
Kotsiubailo L. P., MD, PhD, Assistant of the Department of Infectious Diseases, Shupyk National Medical Academy of Postgraduate Education, Kyiv, Ukraine.
Marchenko O. H., MD, Postgraduate Student of the Department of Infectious Diseases with Epidemiology, Ukrainian Medical Stomatological Academy, Poltava.

Відомості про авторів:
Сизова Л. М., канд. мед. наук, асистент каф. інфекційних хвороб з епідеміологією, Українська медична стоматологічна академія, м. Полтава.
Коваль Т. І., д-р мед. наук, доцент каф. інфекційних хвороб з епідеміологією, Українська медична стоматологічна академія, м. Полтава.
Коцюбайло Л. П., канд. мед. наук, асистент каф. інфекційних хвороб, Національна медична академія післядипломної освіти імені П. Л. Шупика, м. Київ, Україна.
Марченко О. Г., аспірант каф. інфекційних хвороб з епідеміологією, Українська медична стоматологічна академія, м. Полтава.

Сведения об авторах:
Сизова Л. М., канд. мед. наук, ассистент каф. инфекционных болезней с эпидемиологией, Украинская медицинская стоматологическая академия, г. Полтава.
Коваль Т. И., д-р мед. наук, доцент каф. инфекционных болезней с эпидемиологией, Украинская медицинская стоматологическая академия, г. Полтава.
Коцюбайло Л. П., канд. мед. наук, ассистент каф. инфекционных болезней, Национальная медицинская академия последипломного образования имени П. Л. Шупика, г. Киев, Украина.
Марченко Е. Г., аспирант каф. инфекционных болезней с эпидемиологией, Украинская медицинская стоматологическая академия, г. Полтава.

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